REMARKS

Applicants have amended claims 1, 3-5, and 11. New claims 13-20 have been added. Support for the amendments to claim 1 may be found, for example, in Examples 2-7 of the applicants' specification.

Upon entry of this amendment claims 1, 3-8, and 10-20 will be pending with claims 1, 3-8, 10, and 12-20 currently under examination and claim 11 withdrawn from consideration. Applicants respectfully reserve the right of rejoinder of claim 11. No new matter has been added by this amendment.

Previous Objections and Rejections

Applicants acknowledge the withdrawal of the objections to the specification and rejections of claims 5, 6, and 8 under 35 U.S.C. § 112, second paragraph. Applicants also acknowledge the withdrawal of the rejection of claims 1-5 and 8-10 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,210,710 (Skinner) and the rejection of claims 1, 3-5, 8 and 10 as being anticipated by U.S. Patent No. 5,935,604 (Illum).

Claim Rejections under 35 U.S.C. § 103

Claim 1 of the present invention is directed to a controlled-release dosage form suitable for oral administration comprising a matrix. The matrix comprises gellan gum, one or more hydrophilic polymers selected from the group consisting of guar gum, hydroxypropyl methylcellulose, carboxymethyl cellulose sodium salt and xanthan gum, and at least one drug. As amended, claim 1 requires the matrix to be a solid matrix and requires that gellan gum constitute from about 20 to about 50 wt.% of the matrix. The present invention advantageously provides dosage

forms with improved gel stability which are easily formed in vivo, directly in the gastric environment.

Rejection over Skinner

Applicants respectfully request reconsideration of the rejection of claims 1, 3-8, 10 and 12 under 35 U.S.C. § 103(a) as obvious over Skinner.

Skinner discloses sustained release pharmaceutical compositions containing a first component comprising hydroxypropyl cellulose (HPC), ethyl cellulose (EC), or derivatives of HPC, EC or hydroxyethyl cellulose (HEC) with at least one other polymer as a second component. With respect to the second component, Skinner provides an expansive list of over 20 suitable polysaccharides and polymers including, *inter alia*, guar, xanthan gum, and gellan gum. The reference generally discloses that all of the second and subsequent components can be used either alone or as mixtures thereof. See, column 2, line 64 to column 3, line 13 of Skinner.

The Office asserts that the claimed invention is rendered obvious because Skinner mentions that mixtures of second components (i.e., candidate second components from the list including gellan gum and xanthan gum) may be used in combination with the first component. However, applicants submit that to arrive at the invention defined in claim 1 requires an impermissible hindsight selection not taught by Skinner. See MPEP 2142. As noted, for suitable second components, Skinner lists over 20 different polysaccharides along with several classes of synthetic polymers encompassing a host of alternatives. Based on this disclosure, the number of different combinations of the listed second components is legion, and this disclosure of Skinner is devoid of any instruction with respect

to any particular combinations that are preferred or even appropriate. In fact, each example of Skinner demonstrates a blend of a first component and a *single* second component. See, for example, Example 1 in which carboxymethylcellulose (CMC) *or* guar gum is the second component. Based on the foregoing, applicants respectfully submit that Skinner does not include any disclosure or teaching that would lead one skilled in the art to the selection of components required in claim 1 (i.e., the combination of gellan gum and one or more hydrophilic polymers selected from the group consisting of guar gum, hydroxypropyl methylcellulose, carboxymethyl cellulose sodium salt and xanthan gum). Only through impermissible hindsight in view of applicants' disclosure could one skilled in the art arrive at the claimed combination based on the disclosure of Skinner.

As amended, claim 1 also requires that gellan gum constitutes from about 20 to about 50 wt.% of the matrix. As noted, Skinner includes gellan gum along with guar gum and xanthan gum in an exhaustive list of second components to be combined with a first component (i.e., hydroxypropyl cellulose (HPC), ethyl cellulose (EC), or derivatives of HPC, EC or hydroxyethyl cellulose (HEC)). Skinner discloses that the ratio of the first component to the second component should be in the range of from about 1:99 to 99:1, preferably from 5:95 to 95:1, and more preferably from 10:90 to 90:10. However, this disclosure fails to provide one skilled in the art any guidance with regard to the appropriate content of a second component (e.g., gellan gum) when used within a mixture of two or more second components. Moreover, as noted above, neither the general disclosure of Skinner nor the working examples provide any teaching with regard to any combination of more than one second component. Thus, Skinner fails to provide any disclosure

or teaching with regard to the amount of gellan gum to be incorporated into a controlled release dosage form which also contains one or more hydrophilic polymers selected from the group consisting of guar gum, hydroxypropyl methylcellulose, carboxymethyl cellulose sodium salt and xanthan gum, both generally and in the range of from about 20 to about 50 wt.% as required in claim 1, as amended.

In sum, Skinner not only fails to provide one skilled in the art any meaningful disclosure with respect to the selection of the components of the dosage form of claim 1, but also fails to disclose or suggest the required gellan gum content of the solid matrix of the claimed controlled-release dosage form. Accordingly, applicants submit that amended claim 1 is nonobvious over Skinner.

Rejection over Baichwal in view of Skinner

Applicants respectfully request reconsideration of the rejection of claims 1, 3-8, 10 and 12 under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 5,958,456 (Baichwal) in view of Skinner.

Baichwal discloses a sustained or controlled release pharmaceutical formulation comprising a hydrophobic material and a gelling agent. One preferred gelling agent is a combination of a heteropolysaccharide such as xanthan gum and a homopolysaccharide such as locust bean gum. Baichwal discloses that other acceptable gelling agents which may be used are those gelling agents well-known in the art including vegetable gums such as alginates, carrageenan, pectin, guar gum, xanthan gum, modified starch, hydroxypropylmethylcellulose, methylcellulose, and other cellulosic materials such as sodium carboxymethylcellulose and hydroxypropylcellulose. See, for

example, column 6, lines 37-48 of Baichwal. As recognized by the Office, nowhere does Baichwal disclose a controlled-release dosage form comprising gellan gum.

The Office asserts that it would have been obvious to incorporate the gellan gum taught by Skinner within the controlled release formulation of Baichwal. However, Skinner fails to cure the acknowledged deficiency of Baichwal with respect to incorporation of gellan gum. As discussed above, Skinner's mention of gellan gum among numerous other second components and vague disclosure relating to use of mixtures of second components fails to lead one skilled in the art to combine gellan gum with one or more hydrophilic polymers selected from the group consisting of guar gum, hydroxypropyl methylcellulose, carboxymethyl cellulose sodium salt and xanthan gum as required in claim 1. Applicants respectfully submit that relying on this combination of references for disclosing the claimed combination also requires an impermissible hindsight selection in view of applicant's disclosure that is neither disclosed nor suggested by either reference. Moreover, both Baichwal and Skinner fail to provide one skilled in the art any guidance with respect to the claimed gellan gum content of from about 20 to about 50 wt.%. Accordingly, applicants submit that amended claim 1 is nonobvious over Baichwal in view of Skinner.

Rejection over Illum

Applicants respectfully request reconsideration of the rejection of claims 1, 3, 5, 8, 10 and 12 under 35 U.S.C. § 103(a) as obvious over Illum.

Illum discloses a nasal drug delivery composition which provides both an initial rapid release and controlled release of nicotine. The controlled release effect can be achieved by

providing an ion-exchange material that preferably gels when in contact with the nasal mucosa. Suitable polymeric ion-exchange materials include gellan gum, welan, rhamsan, alginate, carboxymethylcellulose, sodium alginate, xanthan, agar, guar derivatives such as carboxymethyl guar gum, carrageenan, dextran sulphate, keratan, dermatan, and pectin. Illum mentions that mixtures of gellan and other polymers such as alginate can be used. In liquid formulations, the polymeric ion-exchange material will typically be provided in a concentration from 0.01% to 20%, preferably 0.05 to 10%, more preferably 0.1% to 5%. See, for example, column 7, lines 29-34, and column 8, lines 17-19 and lines 31-33 of Illum.

At pages 11-12 of the Office action, the Office asserts that the disclosure of Illum renders the present invention *prima facie* obvious because "Illum explicitly teaches a controlled release drug delivery composition comprising polysaccharides and suitable polymeric materials of which include gellan gum, alginate, carboxymethylcellulose (CMC), xanthan gum, agar, guar derivatives and the like."

Applicants have amended claim 1 to require that the controlled-release dosage form suitable for oral administration comprise a **solid** matrix. In contrast, the composition disclosed by Illum is an aqueous nasal spray. One skilled in the art understands that the nasal mucosa and gastro-intestinal system are vastly different environments, especially with respect to drug delivery. One skilled in the art attempting to develop an orally administrable controlled-release dosage form comprising a solid matrix, which reaches the gastric system, would not consider the inapposite teachings of Illum relating to aqueous controlled release nasal sprays formulations.

Moreover, applicants have amended claim 1 to require that gellan gum constitutes from about 20 to about 50 wt.% of the solid matrix. As mentioned above, Illum discloses that in liquid formulations the polymeric ion-exchange material (e.g., gellan gum) will typically be provided in a concentration from 0.01% to 20%, *preferably* from 0.05 to 10%, *more preferably* from 0.1-5%. Also, Examples 5 and 10, which specifically relate to nicotine nasal solutions containing gellan gum, disclose formulations containing only about 2 wt.% or less gellan gum. Accordingly, in addition to being manifestly different from the claimed solid oral dosage forms, the nasal formulations of Illum teach away from formulations requiring higher contents of gellan gum than those specified in Illum and, thus, fail to lead one skilled in the art to a solid matrix comprising about 20 to about 50 wt.% gellan gum as required by claim 1.

Lastly, while Illum mentions that mixtures of gellan with other polymers such as alginate can be used, the reference is silent with respect to any other polymers suitable for use in combination with gellan gum. Applicants submit such vague disclosure by Illum fails to lead one skilled in the art to the claimed combination and would otherwise require an impermissible hindsight selection in view of applicants' disclosure to arrive at the present invention. Furthermore, as noted above, Illum provides no disclosure or teaching of the claimed gellan gum content.

In view of the above, applicants submit that claim 1 is patentable over Skinner, over Baichwal in view of Skinner, and over Illum. Applicants further submit that all claims depending directly or indirectly therefrom are likewise patentable over the cited references for the reasons stated above with respect to claim 1 and for the additional limitations they introduce.

New claims 13-20

New claims 13-17 are directed to the composition of claim 1 wherein the one or more hydrophilic polymers comprises HPMC in various combinations with guar gum, carboxymethyl cellulose sodium salt, and/or xanthan gum. New claims 18-20 are directed to the composition of claim 1 wherein upon wetting the dosage form, a gel is produced for more than 5 hours, more than 24 hours, and more than 1 week, respectively, in gastric fluid simulation. Applicants submit that claims 13-20 are likewise patentable over the cited references for the reasons stated above with respect to claim 1.

The Director is hereby authorized to charge any underpayment, or credit any overpayment, in connection with this response to Deposit Account No. 19-1345.

Respectfully submitted,

/Paul D. Tietz/

Paul D. Tietz, Reg. No. 66,669
SENNIGER POWERS LLP
100 North Broadway, 17th Floor
St. Louis, Missouri 63102
(314) 345-7051

PDT/ACW/slw